

**REMARKS**

Reconsideration of this application is respectfully requested.

Applicants hereby bring to the Examiner's attention that a related application, which is a continuation-in-part of the instant application, is currently pending in the United States Patent & Trademark Office as application serial number 09/441,966. The claims of the related application are similar to the claims of the instant application. At least two Office Actions have issued in the related application.

Claims 1-18 were pending in this application. New claims 19-29 have been added. Support for the new claims can be found, for instance, in original claims 1-18. Claims 1-29 are now pending in this application. No new matter has been added to the application as a result of the present amendment.

Consideration and entry of this amendment are respectfully requested. The Applicants believe that the amendment places the claims into allowable condition or in better form for consideration on appeal. The Applicants do not believe that the amendment creates an undue burden on the Examiner with respect to the search and examination of these claims.

Turning to the instant Office Action, the following objections and rejections are asserted by the Examiner: the drawings stand objected to as informal; claims 1-10 continue to stand rejected under 35 U.S.C. § 102(b) as being anticipated by Rasche et al., *Arzneimittel-Forschung* 25(1), 110-116 (1975) ("Rasche"); claims 3-10 remain rejected under 35 U.S.C. § 103 as being unpatentable over Rasche in view of the state of the art; claims 13, and 16-18 remain rejected under § 103 as being unpatentable over Delaria et al., *J. Biol. Chem.* 1997, 272(18), 12209-12214 ("Delaria") in view of the state of the art as exemplified by Rasche, Fritz et al., U.S. Patent No. 5,407,915 ("Fritz"), and O'Riordan et al., *Am. J. Respir. Crit. Care Med.* Vol. 155, pp. 1522-1528 (O'Riordan"); and claims 1-10, 13, and 16-18 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-10 and 15-18 of copending application number 09/441,966.

Formal drawings are enclosed with this Response. Withdrawal of the objection to the drawings is therefore respectfully requested.

Applicants request that the Examiner hold the obviousness-type double patenting

rejection in abeyance pending allowance of the instant claims. The remaining rejections are addressed below.

Rejection Under 35 U.S.C. § 102

Claims 1-10 stand rejected as being anticipated by Rasche. The Examiner contends that Rasche teaches the use of a Kunitz-type serine protease in a pharmaceutical composition in the treatment of obstructive bronchitis. Applicants respectfully traverse this rejection.

As a general rule, for prior art to anticipate under section 102, every element of the claimed invention must be identically disclosed in a single reference. *Corning Glass Works v. Sumitomo Electric*, 9 USPQ2d 1962, 1965 (Fed. Cir. 1989). The exclusion of a claimed element, no matter how insubstantial or obvious, from a reference is enough to negate anticipation. *Connell v. Sears, Robuck & Co.*, 220 USPQ193, 1098 (Fed. Cir. 1983).

Applicants respectfully submit, as asserted in the Response to the prior Office Action dated December 27, 2002, that the instant claims are not anticipated by Rasche because Rasche does not disclose every element of the claimed invention. Rasche relates to the administration of aprotinin (infusion or inhalation) to subjects who suffer from moderate to severe chronic obstructive bronchitis. The reference states that inhalation of the aprotinin product by patients produces a drop in average airway resistance. However, disclosure of a drop in airway resistance is not a disclosure of a method for accelerating mucociliary clearance, as presently claimed. Thus Rasche, which does not disclose the acceleration of mucociliary clearance, does not teach every element of the claimed invention. Withdrawal of the § 102 rejection of claims 1-10 is therefore respectfully requested.

Applicants further submit that Rasche cannot support a rejection under § 102 of newly added claims 19-29. The newly added claims are directed to a method for accelerating the rate of mucociliary clearance using a Kunitz-type serine protease inhibitor selected from SEQ ID NO:49; SEQ ID NO:2; SEQ ID NO:45; SEQ ID NO:47; SEQ ID NO:71; SEQ ID NO:70; SEQ ID NO:4; SEQ ID NO:5; SEQ ID NO:6; SEQ ID NO:7; SEQ ID NO:3; SEQ ID NO:50; SEQ ID NO:1; SEQ ID NO:52; and SEQ ID NO:8.

Rasche does not disclose such inhibitors. Therefore, claims 19-29 are also not anticipated by Rasche. Allowance of these claims is respectfully requested.

Rejections Under 35 U.S.C. § 103

Claims 3-10 stand rejected as being unpatentable over Rasche in view of the state of the art. The Examiner contents that Rasche provides the motivation for using aprotinin compositions for the treatment of lung conditions and that it would have been *prima facie* obvious to one of ordinary skill in the art to formulate aprotinin in a composition appropriate for administration to human lungs. Applicants respectfully traverse this rejection.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, USPQ2d 1438 (Fed. Cir. 1991). Applicants respectfully submit that one skilled in the art would not have arrived at Applicants' claimed invention based on the teachings of Rasche and the state of the art.

As discussed above, Rasche does not disclose or suggest a method for accelerating the rate of mucociliary clearance. Further, as asserted in the Response to the prior Office Action, Rasche may be considered as *teaching away* from using protease inhibitors for treatment of chronic disease. For instance, Rasche states: "whether a therapy applying the addition of protease inhibitor is reasonable in the long run in chronic diseases *cannot* yet be concluded from these investigations." (Emphasis added). See Rasche at page 116, section 6.. Applicants submit that a person of ordinary skill in the art would not be motivated to provide a method of accelerating MCC, as presently claimed, based on the disclosure of Rasche with any reasonable expectation of success. Accordingly, claims 3-10 are not obvious over Rasche and withdrawal of the § 103 rejection of these claims is respectfully requested.

Additionally, new claim 19-29 are not obvious over Rasche. As noted above, the

new claims are directed to a method for accelerating the rate of mucociliary clearance using a Kunitz-type serine protease inhibitor selected from SEQ ID NO:49; SEQ ID NO:2; SEQ ID NO:45; SEQ ID NO:47; SEQ ID NO:71; SEQ ID NO:70; SEQ ID NO:4; SEQ ID NO:5; SEQ ID NO:6; SEQ ID NO:7; SEQ ID NO:3; SEQ ID NO:50; SEQ ID NO:1; SEQ ID NO:52; and SEQ ID NO:8. Rasche does not disclose or suggest such inhibitors or the use of these inhibitors in a method for accelerating MCC. Therefore, the combination of Rasche with the state of the art also does not teach or suggest Applicants' invention as claimed in new claims 19-29.

Claims 13 and 16-18 stand rejected under § 103 as being unpatentable over Delaria in view of the state of art as exemplified by Rasche, Fritz, and O'Riordan. As discussed in the Response to the previous Office Action, Delaria describes an investigation of various inhibitory properties of recombinant placental bikunin1-170 and both of its synthetically prepared Kunitz domains. However, Delaria makes no mention of mucociliary clearance, or the use of Kunitz-type serine protease inhibitors in the acceleration of mucociliary clearance, as claimed by Applicants. Indeed, Delaria does not teach the use of bikunin1-170 in the treatment of any diseases or conditions, as stated by the Examiner in the prior Office Action (see Office Action of December 27, 2002, see page 7). Fritz, like Delaria, makes no mention of mucociliary clearance, or the use of Kunitz-type serine protease inhibitors in the acceleration of mucociliary clearance. Thus, Fritz adds nothing to Delaria except for Fritz's disclosure of pharmaceutical preparations of serine proteinase inhibitors and the possibility that inhibitors genetically modified as disclosed by Fritz could be effective against neutrophil elastase. However, a disclosure of genetically modified Kunitz-type inhibitors that potentially inhibit neutrophil elastase is not a disclosure of a method for accelerating mucociliary clearance, as presently claimed. There is no suggestion or motivation in either Fritz or Delaria that would lead the skilled artisan to arrive at Applicants' claimed invention.

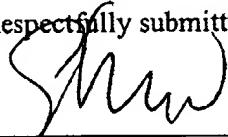
O'Riordan states that neutrophil elastase may contribute to acute antigen-induced mucociliary dysfunction, and generally states that elastase inhibitors may be useful in protecting against mucociliary dysfunction. However, O'Riordan does not contain any specific teachings regarding such inhibitors. Thus, there is no teaching or suggestion in O'Riordan that the Kunitz-type serine protease inhibitors may be useful in accelerating

mucociliary clearance. For at least these reasons, claims, 13 and 16-18 are not rendered obvious by the cited references, and withdrawal of the 35 U.S.C. § 103 rejection is respectfully requested.

Applicants further submit that new claim 19-29 are not obvious over Delaria, Rasche, Fritz, O'Riordan, or combinations of these references. As noted above, the new claims are directed to a method for accelerating the rate of mucociliary clearance using a Kunitz-type serine protease inhibitor selected from SEQ ID NO:49; SEQ ID NO:2; SEQ ID NO:45; SEQ ID NO:47; SEQ ID NO:71; SEQ ID NO:70; SEQ ID NO:4; SEQ ID NO:5; SEQ ID NO:6; SEQ ID NO:7; SEQ ID NO:3; SEQ ID NO:50; SEQ ID NO:1; SEQ ID NO:52; and SEQ ID NO:8. The cited references not disclose or suggest such inhibitors or the use of these inhibitors in a method for accelerating MCC. Therefore, the references do render obvious Applicants' invention as claimed in new claims 19-29.

In summary, Applicants submit that none of the cited references disclose or suggest the claimed methods. The claims, therefore, are not anticipated by, or obvious over, the cited references. Reconsideration and withdrawal of the rejections are respectfully requested. Should the Examiner believe that a discussion of this matter would be helpful, he is invited to telephone the undersigned at (312) 913-0001.

Respectfully submitted,



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